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TO WHOM IT MAY CONCERN:

Be it known that WE, Raghunath Vitthal CHAUDARI, and Sunil Sopana TONDE, citizens of India, residing at National Chemical Laboratory, Pune 411 008 Maharashtra, India, and National Chemical Laboratory, Pune 411 008 Maharashtra, India, respectively, have invented an improvement in

A PROCESS FOR THE PREPARATION OF 2-HYDROXY CARBOXYLIC ACIDS

of which the following is a

SPECIFICATION

CROSS-REFERENCE TO RELATED APPLICATIONS

This is a continuation of International Application No. PCT/IB2003/006202, filed December 26, 2003, which is incorporated by reference herein in its entirety.

FIELD OF THE INVENTION

[0001] The present invention relates to a process for the preparation of 2-hydroxy carboxylic acids. Particularly the present invention relates to a process wherein an enol ester and a hydroxyl compound react with carbon monoxide in presence of a palladium catalyst, containing one or more ligands having one or more coordinating N, O and or P atoms and a solvent at a temperature and a pressure, to produce the 2-acetoxy ester and/or 2-hydroxy ester of the corresponding carboxylic acid, which on further catalytic hydrolysis results in the 2-hydroxy

carboxylic acid. The process has potential importance when applied to vinyl acetate. In a preferred embodiment, vinyl acetate reacts with a hydroxyl compound and carbon monoxide to yield a 2-acetoxy propionic acid or 2-acetoxy propionate ester and/or lactate ester, which can be converted to lactic acid on hydrolysis. Lactic acid is important commercially in various industries, such as baking, cheese, wool dying, resin plasticiser, etc.

BACKGROUND OF THE INVENTION

[0002] Lactic acid has been produced industrially by fermentation of molasses. However, the process is costly and inefficient due to the large amount of byproducts generated by the process. It is the product separation and purification that is expensive. Another commercial source of lactic acid is hydrocyanation of acetaldehyde, followed by hydrolysis of cyanohydrin with H_2SO_4. This method is highly corrosive, consuming stoichometric amount of toxic HCN and H_2SO_4. Furthermore, the process uses expensive HCN and produces stoichometric amount of $(NH_4)_2SO_4$.

[0003] Alkoxycarbonylation of certain aceloxyolefinic compounds is reported in US patents 4,257,973 and 3,857,319.

[0004] German patent 1,221,224 and Swiss patent 589,571 disclose carbonylation of alcohols or phenols with CO and olefins. However, neither patent discloses the alkoxycarbonylation of enol acylates with CO and hydroxyl compound.

[0005] US patent 4,072,709 provides a process for the production of lactic acid, in which alpha-aceloxy-propanaldehyde formed by hydroformylation of vinyl acetate is oxidized to alpha-aceloxy-propionic acid, which is further hydrolyzed to lactic acid. However, the process involves three steps for the formation of lactic acid.

[0006] US patent 4,377,708 provides a process for hydrocarbonylation of vinyl acetate using CO and water as reactants with vinyl acetate. In the process, special precautions are taken to ensure the stability of the catalyst, reactants and products. The process requires the maintenance of a concentration of water at not more than 3 weight percent of the medium to avoid the hydrolysis of reactant vinyl acetate to acetic acid and acetaldehyde.

[0007] European patent 0144188 provides a process for alkoxycarbonylation of enol esters with hydroxyl compounds using Pd, Rh and Ni catalysts and further hydrolysis of the products to hydroxy acids. However, the process operates at a low concentration of hydroxyl compound (<10 times of enol ester). In addition, the process does not provide catalyst separation method and reuse, showing inefficiency of the catalyst.

[0008] Palladium catalyzed hydrocarbonylation of enol esters has been reported in Bull Chem. Soc. Jpn. 69, 1337-1345 (1996). However, the disclosed process requires high pressure of CO (150-250 atm.) and a base, such as pyridine or its derivatives. In addition, loading of the catalyst is high (5 mol% of enol ester) which gives less activity in terms of turn overnumber. Also the process is applicable only for acetoxy esters and hydroxy esters, and not for the important product like hydroxy acids such as lactic acid.

[0009] As can be seen, the prior art processes suffer from several disadvantages such as use of costly and toxic chemicals, formation of large amount of byproducts, low catalyst activity, and catalyst and reactant stability. It is therefore necessary to develop a process for preparation of 2-hydroxy carboxylic acids, which overcomes the drawbacks enumerated above.

[0010] The main object of the present invention is to provide a process for the preparation of 2-hydroxy carboxylic acids, which overcomes the drawbacks of low activity, catalyst stability, use of toxic chemicals, and severe operating conditions.

[0011] Another object of the invention is to provide an efficient catalytic process for the preparation of 2-hydroxy carboxylic acids via carbonylation of enol ester and subsequent hydrolysis of ester of the corresponding 2-acetoxy carboxylic acid and/or ester of the corresponding 2-hydroxy carboxylic acid that operates at milder reaction condition.

[0012] Still another object of the present invention is to provide the methods for catalyst separation and reuse.

SUMMARY OF THE INVENTION

[0013] The present invention relates to a process for preparing a hydroxy carboxylic acid comprising using a palladium catalyst, having one or more ligands containing coordinating nitrogen and/or oxygen and/or phosphorus atoms, to catalyze carbonylation of an enol ester in the presence of a hydroxyl compound to yield 2-acetoxy ester and/or 2-hydroxy ester of the corresponding carboxylic acid at milder reaction conditions, which on further hydrolysis, using acid catalysts, gives a 2-hydroxy carboxylic acid. Both carbonylation and hydrolysis catalysts are reusable.

DETAILED DESCRIPTION OF THE PRESENT INVENTION

[0014] Accordingly the present invention provides a process for the preparation of 2-hydroxy carboxylic acids, comprising

a) Carbonylating an enol ester with carbon monoxide and a hydroxyl compound in the presence of a palladium catalyst comprising an oxygen and/ or nitrogen and/ or phosphorus containing ligand(s) and a solvent, at a temperature in the range of 50-250°C, at a pressure in the range of 50-2000 psig, to obtain a carbonylated ester;

b) hydrolyzing the carbonylated ester with an acid catalyst at a temperature of 10-125°C, to obtain the 2-hydroxy carboxylic acid.

[0015] In an embodiment of the invention, the molar concentration ratio of enol ester to catalyst is in the range of 25:1 to 1,000:1.

[0016] In another embodiment of the invention, the molar concentration ratio of hydroxyl compound and enol ester is not less than one.

[0017] In another embodiment of the invention, the carbonylation catalyst may be recycled for the carbonylation step.

[0018] The enol ester may be an organic compound having formula $R_1C=C(R_2)$-O-Acyl, where R_1 is H or an alkyl group containing 1-5 carbon atoms and R_2 is H or an alkyl group containing 1-5 carbon atoms.

[0019] The hydroxyl compound may be a compound having formula R-OH, where R is H or primary, secondary or tertiary alkyl group containing 1-7 carbon atoms. The hydroxyl compound is preferably selected from the group consisting of water, methanol, ethanol, propanol, iso-propanol, butanol, isobutanol, t-butanol, and pentanol.

[0020] The catalyst may comprise a palladium (II) or palladium (0) compound having formula ABxCy, where A stands for palladium, B is an organic ligand containing one or more

coordinating nitrogen and/or oxygen and/or phosphorus atoms and C is any halogen atom such as F, Cl, Br or I and (x+y) is an integer ranging from 1 to 4, wherein individually x and y can vary in the range of 0 to 4. Such palladium compounds can be selected from the group consisting of palladium chloride, palladium bromide, palladium iodide, and palladium acetate; or a metal complex of palladium such as bis(acetylacetonato)palladium(II), bis(triphenylphosphine)dichloropalladium(II), bis(triphenylphosphine)dibromopalladium (II), bis(triphenylphosphine)diiodopalladium (II), bis(pyridine)dichloropalladium(II), bis(pyridine)didromopalladium (II), bis(pyridine)diiodopalladium (II), bis(acetonotrile)dichloropalladium (II), bis(benzonitrile)dichloropalladium (II), and tetrabis(triphenylphosphine)palladium (0).

[0021] The organic ligand is a compound containing one or more coordinating O atoms selected from the group consisting of acetyl acetonate, salicylaldehyde, p-toluenesulphonic acid, compounds containing one or more coordinating N atoms, such as pyridine, pipyridine, triethyl amine, tributyl amine, quinoline, isoquinoline, 0-phenylenediamine, p-phenylenediamine, ethylenediamine, or coordinating N and O atoms, such as 8-hydroxy quinoline, bis(saliylidene)ethylenediamine, salicylaldoxime, picolinic acid, nicotinic acid, anthranilic acid, one or more P containing compound such as trimethyl phosphine, triethyl phosphine, tri-n-butyl phosphine, tri-t-butyl phosphine, tricyclohexyl phosphine, triphenyl phosphine, bis(dicyclohexylphosphinoethane), bis(dicyclohexylphosphinobutane), bis(diphenylphosphinoethane), bis(diphenylphosphinopropane), bis(diphenylphosphinobutane), bis(diphenylphosphinohexane).

[0022] The solvent may be an organic solvent selected from toluene, benzene, chloroform, dichloromethane, dichloroethane, chlorobenzene, o-dichlorobenzene, p-dichlorobenzene a ketone, e.g. acetone, ethyl methyl ketone, diethyl ketone, acetophenone, a cyclic ether, e.g. tetrahydrofuran, dioxan, or a nitrile, e.g. acetonitrile or benzonitrile.

[0023] In another embodiment of the invention, the carbonylation product is separated by vacuum distillation or solvent extraction using an appropriate solvent, and the carbonylation catalyst is recycled and reused for the carbonylation step.

[0024] Hydrolysis of carbonylation products may be carried out with a catalyst, particularly an acidic catalyst, such as p-toluene sulphonic acid, and aqueous hydrochloric acid, or a resin, such as amberlite, at a temperature in the range of 10-125°C. The catalyst may be separated by distillation or filtration and reused for hydrolysis.

[0025] The process of the invention provides an alternative catalytic system for the production of lactic acid, which is both economic and efficient. The process also provides for catalyst separation and reuse. In addition, the process operates at milder reaction conditions than processes disclosed by the prior art.

EXAMPLES

EXAMPLE 1

[0026] A 50 ml autoclave was charged with the following:

Vinyl acetate:	0.025 mol
Methanol:	0.060 mol
$PdCl_2(PPh_3)_2$:	0.00005 mol
Acetyl acetone:	0.001 mol
Toluene:	20ml

[0027] The contents of the autoclave were flushed thrice with carbon monoxide at room temperature. Thereafter, the contents were heated at 100°C. The autoclave was pressurized with carbon monoxide to 800 psig after the temperature was attained. The contents were stirred for 4 hours continuously. The reactor was then cooled to room temperature and the gas was vented off. The liquid contents were analyzed by gas chromatography. The results of the gas chromatography showed 83.5 % conversion of vinyl acetate with 47.92 % selectivity to methyl-2-acetoxy propionate and 8.0 % selectivity to methyl lactate with turnover number of 210. (TON=Moles of the products hydrolyzable to lactic acid per mole of the catalyst charged).

[0028] The product methyl-2-acetoxy propionate was characterized by ^{1}H-NMR spectroscopy after separation by evaporating the low boilers and solvent and filtering out the precipitated catalyst.

EXAMPLE 2

[0029] A 50 ml autoclave was charged with the following:

Vinyl acetate:	0.025 mol
Methanol:	0.060 mol
$PdCl_2(PPh_3)_2$:	0.00005 mol
Picolinic acid:	0.001 mol
Toluene:	20ml

[0030] The contents of the autoclave were flushed thrice with carbon monoxide at room temperature. Thereafter, the contents were heated at 100°C. The autoclave was pressurized with carbon monoxide to 800 psig after the temperature was attained. The contents were stirred for 10 hours continuously. The reactor was then cooled to room temperature and the gas was vented off. The liquid contents were analyzed by gas chromatography. The results of the gas

chromatography showed 97.66% conversion of vinyl acetate with 61.42% selectivity to methyl-2-acetoxy propionate and 18.98% selectivity to methyl lactate with turn over number of 399.4.

EXAMPLE 3

[0031] Catalyst for recycle run was obtained by filtration after evaporating the low boilers and solvent from the reaction mixture of example 2.

[0032] A 50 ml autoclave was charged with the following:

Vinyl acetate:	0.025 mol
Methanol:	0.060 mol
Catalyst:	recycled from example 2
Picolinic acid:	0.001 mol
Toluene:	20ml

[0033] The contents of the autoclave were flushed thrice with carbon monoxide at room temperature. Thereafter, the contents were heated at 100°C. The autoclave was pressurized with carbon monoxide to 800 psig after the temperature was attained. The contents were stirred for 10 hours continuously. The reactor was then cooled to room temperature and the gas was vented off. The liquid contents were analyzed by gas chromatography. The results of the gas chromatography showed 63.53% conversion of vinyl acetate with 38.08% selectivity to methyl-2-acetoxy propionate and 15.67% selectivity to methyl lactate.

EXAMPLE 4

[0034] A 50 ml autoclave was charged with the following:

Vinyl acetate:	0.025 mol
Methanol:	0.060 mol
$PdCl_2(PPh_3)_2$:	0.00005 mmol
Nicotinic acid:	0.001 mol
Toluene:	20ml

[0035] The contents of the autoclave were flushed thrice with carbon monoxide at room temperature. Thereafter, the contents were heated at 100°C. The autoclave was pressurized with carbon monoxide to 800 psig after the temperature was attained. The contents were stirred for 4 hours continuously. The reactor was then cooled to room temperature and the gas was vented off. The liquid contents were analyzed by gas chromatography. The results of the gas chromatography showed 60.15% conversion of vinyl acetate with 57.57% selectivity to methyl-2-acetoxy propionate and 16% selectivity to methyl lactate with turn over number of 227

EXAMPLE 5

[0036] A 50 ml autoclave was charged with the following:

Vinyl acetate:	0.025 mol
Methanol:	0.060 mol
$PdCl_2(PPh_3)_2$:	0.00005 mol
Anthranilic acid:	0.001 mol
Toluene:	20ml

[0037] The contents of the autoclave were flushed thrice with carbon monoxide at room temperature. Thereafter, the contents were heated at 100°C. The autoclave was pressurized with carbon monoxide to 800 psig after the temperature was attained. The contents were stirred for 10 hours continuously. The reactor was then cooled to room temperature and the gas was vented off. The liquid contents were analyzed by gas chromatography. The results of the gas chromatography showed 98.9% conversion of vinyl acetate with 50.30% selectivity to methyl-2-acetoxy propionate and 20% selectivity to methyl lactate with turn over number of 356.

EXAMPLE 6

[0038] A 50 ml autoclave was charged with the following:

Vinyl acetate:	0.025 mol

Methanol:	0.060 mol
$PdCl_2(PPh_3)_2$:	0.00005 mol
Pyridine:	0.001 mol
p-toluenesulphonic acid:	0.0002 mol
Toluene:	20ml

[0039] The contents of the autoclave were flushed thrice with carbon monoxide at room temperature. Thereafter, the contents were heated at 100°C. The autoclave was pressurized with carbon monoxide to 800 psig after the temperature was attained. The contents were stirred for 4 hours continuously. The reactor was then cooled to room temperature and the gas was vented off. The liquid contents were analyzed by gas chromatography. The results of the gas chromatography showed 99% conversion of vinyl acetate with 76.45% selectivity to methyl-2-acetoxy propionate with turn over number of 411.

EXAMPLE 7

[0040] A 50 ml autoclave was charged with the following:

Vinyl acetate:	0.025 mol
Methanol:	0.060 mol
$PdCl_2(PPh_3)_2$:	0.00005 mol
Triphenylphosphine:	0.001 mol
Toluene:	20ml

[0041] The contents of the autoclave were flushed thrice with carbon monoxide at room temperature. Thereafter, the contents were heated at 100°C. The autoclave was pressurized with carbon monoxide to 800 psig after the temperature was attained. The contents were stirred for 8 hours continuously. The reactor was then cooled to room temperature and the gas was vented off. The liquid contents were analyzed by gas chromatography. The results of the gas chromatography showed 99% conversion of vinyl acetate with 2% selectivity to methyl-2-acetoxy propionate with turn over number of 10.

EXAMPLE 8

[0042] A 50 ml autoclave was charged with the following:

Vinyl acetate:	0.025 mol
Methanol:	0.060 mol
$PdCl_2(PPh_3)_2$:	0.00005 mol
p-toluenesulphonic acid:	0.0002 mol
Acetyl acetone:	0.001 mol
Tetrahydrofuran	20ml

[0043] The contents of the autoclave were flushed thrice with carbon monoxide at room temperature. Thereafter, the contents were heated at 100°C. The autoclave was pressurized with carbon monoxide to 800 psig after the temperature was attained. The contents were stirred for 4 hours continuously. The reactor was then cooled to room temperature and the gas was vented off. The liquid contents were analyzed by gas chromatography. The results of the gas chromatography showed 91.43% conversion of vinyl acetate with 35.67% selectivity to methyl-2-acetoxy propionate and 25.65% selectivity to methyl lactate with turn over number of 295.

EXAMPLE 9

[0044] A 50 ml autoclave was charged with the following:

Vinyl acetate:	0.025 mol
Methanol:	0.060 mol
$PdCl_2(PPh_3)_2$:	0.00005 mol
Acetyl acetone:	0.001 mol
p-toluenesulphonic acid:	0.0002 mol
Tetrahydrofuran	20ml

[0045] The contents of the autoclave were flushed thrice with carbon monoxide at room temperature. Thereafter, the contents were heated at 100°C. The autoclave was pressurized with carbon monoxide to 800 psig after the temperature was attained. The contents were stirred for 4 hours continuously. The reactor was then cooled to room temperature and the gas was vented

off. The liquid contents were analyzed by gas chromatography. The results of the gas chromatography showed 82.65% conversion of vinyl acetate with 4% selectivity to methyl-2-acetoxy propionate and 42.56% selectivity to methyl lactate with turn over number of 202.

EXAMPLE 10

[0046] A 50 ml autoclave was charged with the following: .

Vinyl acetate:	0.025 mol
Methanol:	23 ml
$PdCl_2(PPh_3)_2$:	0.00005 mol
Acetyl acetone:	0.001 mol

[0047] The contents of the autoclave were flushed thrice with carbon monoxide at room temperature. Thereafter, the contents were heated at 100°C. The autoclave was pressurized with carbon monoxide to 800 psig after the temperature was attained. The contents were stirred for 3 hours continuously. The reactor was then cooled to room temperature and the gas was vented off. The liquid contents were analyzed by gas chromatography. The results of the gas chromatography showed 91.26% % conversion of vinyl acetate with 3% selectivity to methyl-2-acetoxy propionate with turn over number of 10.97.

EXAMPLE 11

[0048] Methyl lactate was separated by extracting with 15 ml water from the reaction mixture of example 3, to which 1 ml of conc. HCI was added. Thereafter, the reaction mixture was refluxed for 3 hours. The contents were analyzed by gas chromatography after cooling the reaction mixture. The results showed 58 % conversion of methyl lactate.

EXAMPLE 12

[0049] 0.191 g of p-toluene sulphonic acid and 15 ml water was added to 1.46 g of methyl-2-acetoxy propionate. Thereafter, the reaction mixture was refluxed for 3 hours and the contents were analyzed by gas chromatography after cooling the reaction mixture. The analysis showed 100% conversion of methyl-2-acetoxy propionate with 100% selectivity to lactic acid.

EXAMPLE 13

[0050] 15 ml of water and 0.1g of amberlite IR 20 resin were added to the reaction mixture of example 4. Thereafter, the contents were heated to 80°C. for 3 hours. The contents were analyzed by gas chromatography. The analysis showed 17.33% conversion of methyl-2-acetoxy propionate.

EXAMPLE 14

[0051] The catalyst from example 13 was separated by filtration and added to 1.44 g of methyl-2-acetoxy propionate and 15 ml water. Thereafter the contents were heated to 80°C for 3 hours. The analysis was done by gas chromatography. The results showed 41.77% conversion of methyl-2-acetoxy propionate with 100 % selectivity to lactic acid.

[0052] The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description. Such modifications are intended to fall within the scope of the appended claims. Various references are cited herein, the disclosure of which are incorporated by reference in their entireties.